Paper No. 28

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte TINA ETCHEVERRY and THOMAS RYLL

Appeal No. 2002-0872
Application No. 08/470,849

ON BRIEF

Before SCHEINER, ADAMS and MILLS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 18-23. The only other pending claim (claim 24) was objected to as dependent upon a rejected base claim and was not included as part of this appeal.

Claims 18 and 20 are illustrative of the subject matter on appeal and are reproduced below:

18. A human TNFR1-IgG_1 preparation comprising TNFR1-IgG_1 prepared by a process comprising:
    (a) culturing a mammalian dp12.CHO host cell which expresses a human TNFR1-IgG_1 chimera in a growth phase under such conditions and for a period of time such that maximum cell growth is achieved;
    (b) culturing the host cell in a production phase:
        (1) in the presence of sodium butyrate at a concentration of about 1 mM to about 6 mM;
        (2) at an osmolality of about 350-450 mOsm; and
        (3) at a temperature about between 30°C and 35°C.

20. A human TNFR1-IgG_1 preparation comprising human TNFR1-IgG_1 molecules wherein the TNFR1-IgG_1 molecules have a molar ratio of sialic acid to protein of about 4-7.

The references relied upon by the examiner are:

Beutler et al. (Beutler) 5,447,851 Sep. 5, 1995

Ashkenazi et al. (Ashkenazi), "Protection against endotoxic shock by a tumor necrosis factor receptor immunoadhesin," Proc. Natl. Acad. Sci., USA, Vol. 88, pp. 10535-39 (1991)

GROUNDS OF REJECTION

Claims 18-23 stand rejected under 35 U.S.C. § 102(b) as anticipated by Ashkenazi.

Claims 18-23 stand rejected under 35 U.S.C. § 102(e) as anticipated by Beutler.

We reverse.

DISCUSSION

Ashkenazi:

According to the examiner (Answer, page 4[1]), Ashkenazi teach a recombinant TNFR1-IgG_1 protein produced in human embryonic kidney 293 cells. See also Ashkenazi, page 10535, column 2, "materials and methods." The examiner argues (Answer, bridging paragraph, pages 4-5):

> Since neither the prior art nor the specification provide any evidence that the recombinantly produced human tumor necrosis factor receptor immunoglobulin chimeric protein in CHO cells possesses any different properties than any other recombinant tumor necrosis factor receptor immunoglobulin chimeric protein isolated from HEK293 cells, the protein of Ashkenazi et al. can reasonably be considered to be same [sic] absent any evidence to the contrary.

[1] The Answer does not contain page numbers. For administrative convenience we refer to pages of the Answer as if the Answer were numbered consecutively starting with the first page, page number 1.

In addition, the examiner finds (Answer, page 5), "[c]laims 20-23 are directed to human tumor necrosis factor receptor immunoglobulin chimeric protein isolated from the process of claims 18-19 which results in specific glycosylation properties." According to the examiner (id.), "[t]hese glycosylation limitations of molar ratios of sialic acid and N-acetylglucosamine are inherent properties of the glycosylated [sic] of human tumor necrosis factor receptor immunoglobulin chimeric protein and the protein of Ashkenazi et al. can reasonably be considered to be same [sic] absent any evidence to the contrary."

However, as appellants point out (Brief, page 4, emphasis removed), "Ashkenazi et al. do not disclose the specific culturing conditions used; such as the temperature at which the cells are grown and/or held in a production phase, the osmolality of the media, or the sodium butyrate concentrations of the media." Appellants emphasize (Brief, pages 5-6), "that when the cell culture process is altered by the use of separate growth and production phases, and when alterations are made in the production phase of cell culture, variation in the oligosaccharide component of an expressed glycoprotein will result." In support of this argument appellants rely on Goochee (U.S. Patent No. 5,510,261), and Tables I-V of their specification.

In response, the examiner argues (Answer, page 6), "no evidnece [sic] has been presented that the claimed genus of human tumor necrosis factor receptor immunoglobulin chimeric protein is glycosylated differently in CHO cells versus the HEK 293 cells. Furthermore, the claims are directed to product[-]by[-]process or range limitations of the glycosylation and not a specific species.

In considering the examiner's position, we believe the statement of the rejection resulted from a misapplication of the principles enunciated in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977) (footnote omitted), where the court stated:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.... Whether the rejection is based on 'inherency' under 35 U.S.C. § 102, on 'prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products.

Best is directed to a particular set of circumstances where examiners in the USPTO cannot readily determine whether a difference exists between the subject matter of a given claim and a particular prior art document. However, in order to invoke the principles of Best, the examiner must first make factual findings which support the conclusion that the claimed and prior art products prima facie are "identical or substantially identical." This determination, however, must be made on a case-by-case basis, based upon the facts in the individual case.

We do not find the examiner has adequately established under the principles of Best, a prima facie case that the claimed and prior art products are "identical or substantially identical" to appropriately shift the burden to appellant to establish a patentable distinction between the claimed and referenced methods. On this record, appellants provide evidence of the arts' recognition that "glycoproteins from a single cell line are likely to show varying carbohydrate structures due to variations in the cell culture process used…." Brief, page 5. In addition, appellants' specification discloses that variations in culture conditions result in variations in the oligosaccharide component of an expressed glycoprotein. See id. In contrast, as appellants point out (Brief, page

4), Ashkenazi not only teaches a different cell line, but also fails to identify the conditions used to produce their TNFR1-IgG_1 fusion protein in HEK 293 cells. Based on the evidence of record, it is our opinion that the examiner failed to met his burden of establishing that the TNFR1-IgG_1 preparation of Ashkenazi would be the same or substantially similar to appellants' claimed INFR1-IgG_1 preparation. Stated differently, the examiner has not established that despite appellants' evidence that different cell lines and culture conditions result in different glycosylation patterns, the Ashkenazi TNFR1 IgG_1 preparation would be expected to be the same or substantially the same as appellants' TNFR1 IgG_1 preparation.

Furthermore, to the extent the examiner relies on the concept of inherency, we remind the examiner that "[i]nherency … may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). In our opinion, based on the evidence of record, the examiner failed to provide sufficient evidence that the culture conditions, and HEK 293 cell line taught by Ashkenazi would inherently produce a TNFR1-IgG_1 protein that is "inherently the same" as that claimed by appellants.

In addition, we recognize the examiner's statement (Paper No. 18, page 3), "[c]laim 24 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims." For emphasis, claim 24 is reproduced below:

> 24. The human TNFR1-IgG_1 preparation of Claim 20 wherein the molar ratio of sialic acid to protein is of about 5 to 6.

In our opinion, the indication that claim 24 would be allowable if re-written in independent form is inconsistent with the continued rejection of claims 20-23 on appeal. Each of claims 20-23 are drawn to a human TNFR1-IgG_1 preparation with various limitations as to moles of either N-acetylglucosamine or sialic acid residues per mole of TNFR1-IgG_1 protein. The examiner offered no explanation as to why claim 24 would be allowable while the rejection should be maintained for claims 20-23.

For the foregoing reasons we reverse the rejection of claims 18-23 under 35 U.S.C. § 102(b) as anticipated by Ashkenazi.

Beutler:

According to the examiner (Answer, page 5), Beuler "teach the preparation of the recombinant human tumor necrosis factor receptor immunoglobulin chimeric protein produced in CHO cells (column 4, lines 49-62; column 8, line 26-28; column 9, lines 45-68)." However, as appellants' point out (Brief, page 11), "[t]he protein of Beutler et al. simply is not a 'human TNFR1-IgG_1' as that term is used in the specification and claims of the present application, it is a mixed human-mouse chimeric protein and is thus outside the claims of this application." In this regard, we note that appellants' TNFR1-IgG_1 construct is fusion of human type 1 TNFR and human IgG1 sequences beginning at aspartic acid 216. See Specification, pages 34-35.

It may, however, be that the examiner believes that the claim reads on a human TNFR1 – mouse IgG_1 fusion protein. This, however, as appellants point out, is contrary to the use of the term "human TNFR1-IgG_1 as it is used in appellants' specification. See supra. As set forth in Standard Oil Company v. American Cyanamid Company, 774 F.2d 448, 452, 227 USPQ 293, 296 (CAFC 1985):

> the prosecution history (sometimes called "file wrapper and contents") of the patent consists of the entire record of proceedings in the Patent and Trademark Office. This includes all express representations made by or on behalf of the applicant to the examiner to induce a patent grant, or, as here, to reissue a patent. Such representations include amendments to the claims and arguments made to convince the examiner that the claimed invention meets the statutory requirements of novelty, utility, and nonobviousness. Thus, the prosecution history (or file wrapper) limits the interpretation of claims so as to exclude any interpretation that may have been disclaimed or disavowed during prosecution in order to obtain claim allowance.

In our opinion, appellants limited the interpretation of their claimed invention to a human TNFR1 – human IgG_1 preparation, by amending their claimed invention to include the term "human" in front of the term TNFR1-IgG_1 (see Paper No. 8, page 2), and by arguing that their claimed invention is limited to human TNFR1 – human IgG_1 preparations (see Paper No. 8, page 6, and Brief, page 11). Accordingly, the human-mouse construct disclosed by Beutler does not anticipate the claimed invention.

We recognize the examiner argument (Answer, page 12), "[t]he claims are not limited to a specific species with a specific amino acid sequence, but is [sic] encompass a genus of 'human TNFR1-IgG' whose amino acid sequence is not limited." The examiner, however, has not explained why the absence of amino acid sequence information would have any effect in the determination of whether a chimeric human-mouse fusion protein anticipates a human fusion protein as set forth in the specification and claims (e.g., claim 18, "[a] human TNFR1-IgG_1 preparation…."). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). It is

therefore the examiner's burden of establishing that human-mouse construct disclosed by Beutler is expressly or inherently the same as the construct set forth in appellants' claims. This the examiner has not done.

For the foregoing reasons we reverse the rejection of claims 18-23 under 35 U.S.C. § 102(e) as anticipated by Beutler.

REVERSED

Toni R. Scheiner Administrative Patent Judge	)
	) BOARD OF PATENT
Donald E. Adams Administrative Patent Judge	) APPEALS AND
	) INTERFERENCES
Demetra J. Mills Administrative Patent Judge	)

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